Influence of Degree of Polymerization on Behavior of Cellulose During Homogenization and Extrusion/Spheronization

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ABSTRACT The study objective was to investigate the influence of the degree of polymerization (DP) of cellulose materials (microcrystalline cellulose [MCC] and powder cellulose [PC]) on the behavior of these materials during homogenization and extrusion/spheronization processes. Suspensions of the cellulose types with different DP values were homogenized using a high-pressure homogenizer. The particle size, agglomeration index, and apparent viscosity of these suspensions was determined at different times after pouring. Additionally, these different cellulose types were processed into pellets using the extrusion/spheronization method, and the water content and power consumption as a function of the DP were determined. Cellulose types with a high DP value showed greater particle size after homogenization than the types with a low DP value. In contrast, no relevant relationship between the apparent viscosity and DP could be observed. During the extrusion process, water content in the extrudate and pellet porosity were increased as the DP was increased for the extrudates produced at the same level of power consumption. MCC types with various DPs compared with PC provided a novel way of understanding the role of cellulose in the extrusion process. The DP showed a remarkable influence on the physicochemical properties of the cellulose materials and, consequently, on the behavior of these materials during the extrusion/spheronization process. It is postulated that the sponge model is more appropriate for the cellulose type with high DP (PC), whereas the gel model is more applicable to cellulose types with lower DP (MCC).

INTRODUCTION

Pellets of uniform size, low porosity, and regular shape can be produced via a properly formulated and conducted extrusion/spheronization process (1,2). Microcrystalline cellulose (MCC) is the most commonly and widely used excipient in this process because of its physical properties (3). In contrast, powdered cellulose (PC) is much less suitable for pelletization by extrusion/spheronization (4,5), despite its similar chemical structure.

The unique functionality of MCC is still not fully understood. Water, which is well known to play a crucial role in the process, is usually used as a granulation fluid (6-8). The amount and distribution of the granulation liquid in the wet mass during the extrusion process are critical to the success of the spheronization procedure that follows (9,10). The movement of water during extrusion may play a critical role for ram extruders (11), whereas it is less important for continuously operating extruders like twin-screw extruders (1). The "sponge" model (12) and the "crystallite-gel" model (13) represent 2 recent

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proposed to explain the way in which the free water is held in the wet stage during this process.

The extrusion process and the end-product properties depend a great deal on the type and the physicochemical properties of the cellulose materials (4,5). If all other variables are kept constant, different types of MCC result in pellets of different sizes and shapes (14,15). Most conventional types of MCC have a DP of about 230. Recently, high-density MCCs have become available on the market, which have a lower DP. However, there is a lack of information regarding whether the DP of MCC is relevant for the functionality of MCC during extrusion/spheronization.

In previous studies, we found that the application of high-pressure homogenization or extrusion reduced the particle size of the PC types to a minor extent, which led to a significant decrease in the particle size of MCC types; consequently, it was not possible to extrude most types of cellulose powder (16,17). Regarding the MCC types, it was found that using colloidal-grade or high-density MCC resulted in pellets with different properties than the other types (17). It was proposed that this different behavior could be attributed to the shape, crystallinity index, and degree of polymerization (DP) of the MCC used. However, it was found that the crystallinity differs greatly only between PC and MCC types, whereas no great difference was observed between the tested MCC types (16,18).

Therefore, the overall study objective is to investigate the effect of the DP of cellulose materials on the behavior of these materials during the homogenization process and their effect on the properties of the produced pellets. In order to perform a systematic study, cellulose types with different DP were investigated. It was possible to include 7 different types of MCC with DP varying between 166 and 365 in this study. Therefore, several batches of experimental MCCs of different DP were compared to commercially available MCCs and 1 type of PC.

MATERIALS AND METHODS

Materials

Avicel PH 101 (MCC, DP 225) and Avicel PH 301 (MCC, DP 166) were supplied by FMC (Philadelphia, PA). A type of powdered cellulose (Elcema P050, PC, DP 1431) was furnished by Degussa (Frankfurt am Main, Germany). Experimental MCC types with different polymerization grade, namely DP 190, DP 245, DP 299, DP 345, and DP 365, were donated from Microcellulose Weissenborn (Weissenborn, Germany). Their DP will code the cellulose types.

Properties (mean particle size, degree of crystallinity [CI], and DP) of the different types tested are listed in Table 1. The CI of the MCC types varied in a small range from 67.1% to 75.4%. The PC types had both a high DP and a low CI compared to the MCC types.

Table 1. Properties of Microcrystalline Cellulose the Various Investigated Cellulose Types

Cellulose Type	Degree of Polymerization	Crystallinity Index	Mean Diameter* [µm]	Mean Diameter** [µm]
MCC	166	75.4	22.5	52.9
MCC	190	74.5	22.2	114.0
MCC	225	68.9	22.5	51.5
MCC	245	74.1	24.3	61.5
MCC	299	71.1	27.8	61.0
MCC	345	67.1	26.9	54.7
MCC	365	71.8	26.7	109.4
PC	1431	35.8	27.3	30.7

**Mean particle size [D_{50}] of 9% presuspension before the homogenization.*

***Mean particle size [D_{50}] of dry cellulose powder.*

EXPERIMENTAL SECTION

Powder Evaluation

X-Ray Diffraction Evaluation

The crystallinity was assessed using an X-ray diffractometer (Stoe Cie, Darmstadt, Germany) with a rotating anode, and the crystallinity index was calculated according to Knolle and Jayme (19). The transmission technique was carried out with copper-k α radiation monochromatized at a wavelength of 1.5405 Å. All measurements were carried out with a voltage of 40 kV and a current of 200 mA. The samples were scanned over the region of 5° to 50° 2 Theta with the speed of 1° 2 Theta per 10 seconds, and the signals were detected by a position sensitive detector.

Determination of the Degree of Polymerization

The degree of polymerization was determined according to *European Pharmacopoeia* (20). The viscosity of a solution of cellulose is determined through a 1-point measurement with a capillary type viscosimeter.

Homogenization Process

Preparation of the Suspensions

The preparation method of the cellulose suspensions has been described elsewhere (15). Briefly, 9 g of the tested cellulose (with a different DP) was dispersed in 100 mL double distilled water using a magnet stirrer and then 40 mL of this suspension was treated with an Ultra-Turrax T25 (Jahnke & Kunkel, Staufen, Germany) for 3 minutes to achieve a homogeneous presuspension. The presuspension was then homogenized using a high-pressure homogenizer (Micron Lab 40; APV Gaulin, Lübeck, Germany) at a pressure of 40 MPa with 2, 4, and 6 cycles. Formulations were prepared in duplicate.

Some homogenized suspensions (4 cycles, 40 MPa) were filtered, the filter cakes were dried under ambient conditions, and photographs of them were taken.

Suspension Evaluation

Particle Size Analysis

The particle size and size distribution measurements of the suspensions were carried out using a laser diffraction analyzer (Helos, Sympatec, Clausthal-Zellerfeld, Germany) at a focal length of 50 mm, corresponding to a measurement range of 0.45µm to 100 µm. An aliquot of the suspension was dispersed into a stirred sample filled with deionized water. It is well known that the microcrystalline cellulose showed a marked aggregation tendency after the application of mechanical shear (15); therefore, the measurements were performed before and after treatment with the ultrasonic (60 W, 40 kHz). A short appropriate sonication time was chosen (90 seconds) because the cellulose fibers are reported to be broken by ultrasonic treatment (21). The short sonication will affect the MCC agglomerates only, without significantly affecting the cellulose chain (22). Three measurements were made on each suspension before and after the treatment with the ultrasonic.

The agglomeration behavior of MCC can be estimated by calculating the agglomeration index, which is the ratio of mean diameter (D_{50}) before and after sonication (23). Very little agglomerated suspension displayed an agglomeration index close to 1.

The resulting particle size distributions were averaged. The emulsions were characterized by the D_{99} and the D_{50} quantiles of the volumetric distribution. D_{50}, mean diameter, is defined as the size at which 50% of the particles are smaller. D_{99} is defined as the size at which 99% of the particles are smaller.

Determination of the Apparent Viscosity

A rotation viscometer (Rheoanalyzer; Contraves, Gieres, France) equipped with coaxial cylinders was used to measure the apparent slurry viscosity. An MS-DIN 114 unit was used for the homogenized suspensions, whereas an MS-DIN 125 unit was used for the nonhomogenized one. The rate of shear was increased up to 488 seconds^{-1}, and the apparent

viscosity was calculated from the recorded shear stress at 488 seconds^{-1}. Two samples of the same suspension were investigated; each sample was then measured twice and the results were averaged.

Pelletization Process

Production of Pellets

The pellets were made by extrusion/spheronization. The materials were extruded in a twin-screw extruder, spheronized, and dried using the equipment described earlier (1). The powder feeding rate was set at 25 ± g/minute^{-1} and the screw speed at 60 revolutions/minute^{-1}. The extrusion was performed first at a desired power consumption of 200 W. The settings for the process variables resulted in acceptable pellets using standard types of MCC. The desired power consumption was changed if the pellets produced at 200 W were of inferior quality. After reaching the steady state, 500 g of the extrudates were collected, spheronized, and dried. During the extrusion, 3 samples of the extrudates were taken and dried in an oven at 105°C for at least 24 hours in order to determine their water content.

Characterization of Pellets

Diameter and Shape

The mean Feret diameter and the aspect ratio of at least 500 pellets of each batch were measured using a Leco 2001 image analysis system (Leco Instruments, St. Joseph, MI), as described earlier (23). For each cellulose type, the batch with the lowest aspect ratio was used for further characterization.

Fracture Force

The sieve fraction between 900 µm to 1,000 µm was stored for at least 2 days in a relative air humidity of 55%. Subsequently, the fracture force of at least 50 pellets of each type was measured with a Texture Analyser (TA-XT2; Stable Micro Systems, Haslemerle, Surrey, UK).

Density and Porosity

The apparent particle density of the cellulose powders was determined using a helium pycnometer (Accupyc 1330; Micromeritics, Norcross, GA). The apparent pellet density was determined by mercury pycnometry (Pascal 140; CE Instruments, Rodano, Italy). These 2 densities were used to calculate the porosity of the pellets.

RESULTS

Effect of Polymerization Degree on Cellulose Behavior During Homogenization

The behavior of the cellulose material during homogenization was compared with the results of extrusion process, because during the extrusion process, shear forces act on the cellulose particle. In our previous work, we studied the effect of homogenization parameters (pressure and number of cycles) of different concentrations of MCC on the physicochemical properties of the MCC suspensions (16). It was found that the particle sizes of the suspensions homogenized at 40 MPa and 6 cycles corresponded well with the particle size after the extrusion process. Therefore, all suspensions were homogenized at this pressure with different cycles.

Figure 1 shows that most cellulose types behaved similarly, and no noticeable distinction among them could be observed.

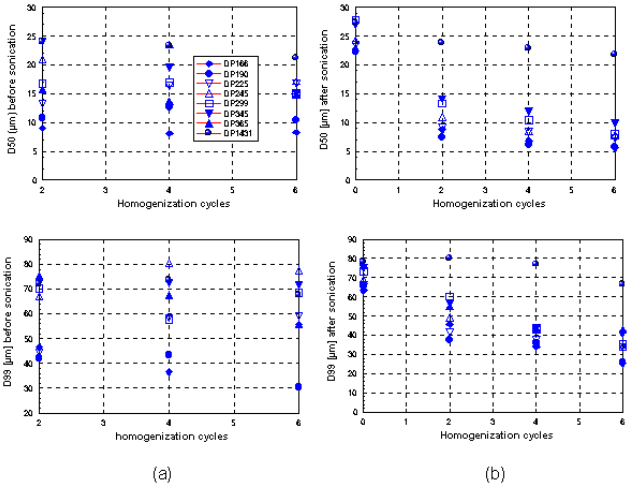

Figure 1. Cellulose behavior (microcrystalline and powdered) with various degree of polymerization values during the homogenization process after different cycles at 40 MPa.

Passing the suspension through the homogenizer additional times resulted in the formation of largely agglomerated particles (Figure 1a), which were disaggregated after the application of sonication (Figure 1b). The single exception was the behavior of the cellulose type with a DP value of 1341 (Elcema P050) because an imperceptible difference in particle size was observed either before or after the sonication. Increasing the number of pouring times also had no noticeable effect. This behavior was also reflected in the agglomeration index values (after 6 homogenization cycles). The agglomeration index was found to be 1.47, 1.81, 2.33, 2.19, 1.89, 1.54, and 1.47 for DP166, DP190, DP226, DP245, DP299, DP345, and DP365, respectively, whereas an agglomeration index of 1.02 was found for DP1341, indicating no agglomeration.

Plotting the particle size (D_{50} and D_{99} after sonication) of the cellulose suspensions against their DP values (Figure 2) clearly shows that there is a significant correlation between the suspension particle sizes and the DP values of the different MCCs (R^2 values are 0.9650 and 0.9247 for D_{50} and D_{99}, respectively), with the cellulose with the higher DP value showing a greater particle size.

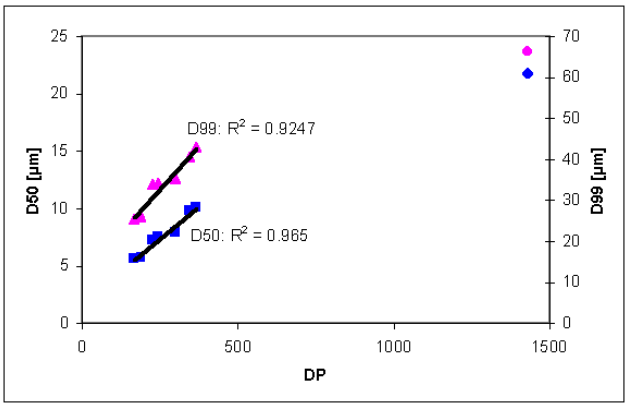

Figure 2. Correlation between the particle size and the degree of polymerization values after the homogenization process (6 cycles, 40 MPa).

The D_{50} and D_{99} values for the PC are higher, as can be expected from the DP, but the values cannot be described well by the regression line.

The homogenization process influenced the apparent viscosity of the different cellulose types, and a concomitant increase in apparent suspension viscosity was observed for all types as the pouring time was increased (Figure 3).

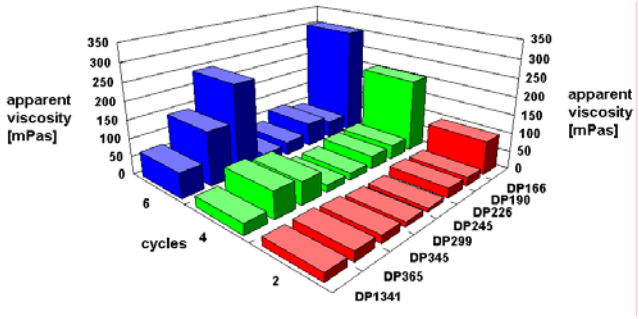

Figure 3. Influence of homogenization cycles at 40 MPa pressure on the apparent viscosity of different microcrystalline and powdered cellulose types.

The 2 MCC types with a DP of 166 and 345 showed the highest increase in apparent viscosity. They were prepared from hardwood, whereas the other MCC types were derived from softwood. For the increase in apparent suspension viscosity, the origin of the material seems to be of higher importance compared to the DP (Figure 2). A shear-thinning behavior dependent on the shear rate was observed for all MCC types, their suspensions liquefying reversibly upon shaking and solidifying upon standing. DP 1341 displayed a behavior less dependent on rate of shear (16).

Clearly, the dried filter cakes of homogenized suspensions had different appearances (Figure 4).

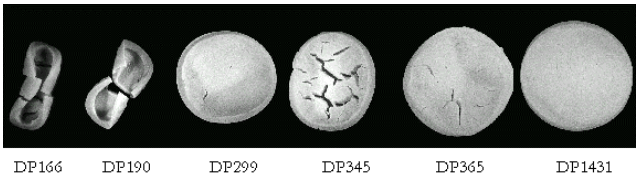

Figure 4. Dried filter cakes of homogenized suspensions of different cellulose types.

The PC cake did not undergo any changes in its shape after drying, and it was porous and weak.

However, decreasing the DP value resulted in a higher shrinking tendency after drying, as the body for a low DP cellulose is highly deformed and presents a strong structure. These marked differences were observed among the homogenized suspensions only, whereas no obvious difference was noticed among the nonhomogenized suspensions with either low or high DP value.

Effect of Degree of Polymerization on Extrusion/Spheronization and Pellet Characteristics

Extrusion/Spheronization Process

The cellulose types were first extruded at a desired power consumption of 200 W and spheronized afterwards. This level of power consumption was found in earlier works to be optimal for the production of pellets made of standard types of MCCs (eg, Avicel PH types). At this desired power consumption, some of the tested types did not yield satisfactory pellets in terms of aspect ratio. DP 166 was easily extrudable but yielded very big agglomerates, and it had to be extruded at 250 W in order for it to yield satisfactory pellets. These pellets were, however, not of an optimum quality, ie, the aspect ratio exceeded 1.1. DP 190 and also yielded at 200 W an overwetted extrudate. An increase of 20 W in the power consumption caused a shift from a slightly wet extrudate to a slightly dry extrudate that yielded doubled pellets, suggesting that this type of MCC could be sensitive to slight changes in water content. The extrusion of DP 226 and DP 245 proceeded without problems during extrusion at 200 W, and rounded pellets were yielded.

DP 299, DP 345, and DP 365 caused some problems during extrusion. Some of the 48 extrusion dies were occasionally obstructed. In the case of DP 299, however, the extrusion process had to be aborted after a while. Regarding DP 345 and 365 types, the water pump was adjusted to work at maximum frequency and volume in order to deliver enough fluid to keep the power consumption at the desired level. This adjustment caused small differences in the power consumption between batches because the system was no longer able to stabilize the power consumption by adjusting the water feed rate.

The same problems intensified with DP 1431. Thus, the powder feeding rate for this cellulose was set to 20 g ± 1 g. Although the water pump was operating at maximum frequency, it was not possible to get the power consumption below 240 W. The obstruction of the dies was stronger, and the barrel of the extruder slowly filled up with wet granulate that gradually pushed the granulation water backward. The powder then accumulated in its feeding opening, hindering further powder feeding. Consequently, the process was aborted for 2 batches. Only 1 batch later did it become possible to restore the process working long enough to obtain extrudate samples for further processing (17).

Pellet Properties

Figure 5 shows the water content of the extrudates produced at a desired power consumption of 200 W for MCC types and 240 W for PC. There is a strong correlation between DP of MCC and the water content of the extrudate ($R^2 = 0.942$). The changes in the level of power consumption necessary to produce suitable pellets had only a minor influence on the level of water content (max 5%). These differences in water content are inconsequential compared to the differences shown in Figure 5.

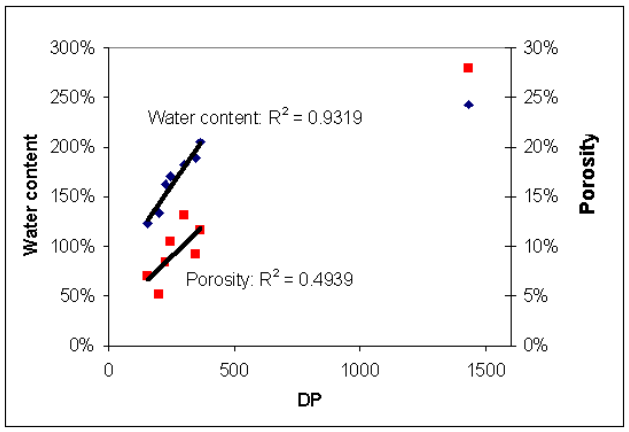

Figure 5. Effect of the degree of polymerization of the used cellulose on the extrudate water content and pellet porosity.

Porosity of the pellets made from different types of MCC is poorly correlated with the DP (Figure 5). However, pellets obtained from PC showed a much higher porosity compared to MCC pellets. When all

cellulose types are considered, a certain relation between porosity and DP can be seen.

Fracture force of the pellets seems not to be correlated with DP (Figure 6). Pellets prepared from powdered cellulose showed the same fracture force as those made from MCC.

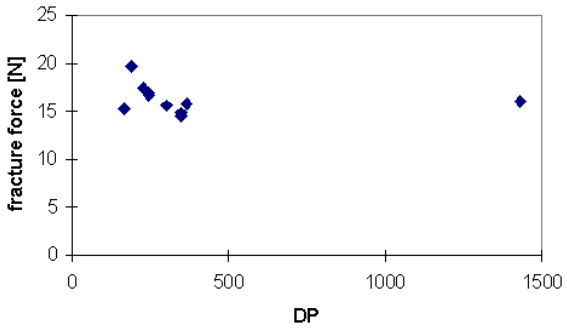

Figure 6. Influence of the degree of polymerization on the fracture force.

DISCUSSION

Two models were proposed recently in the literature to explain the behavior of MCC during the extrusion/spheronization process, namely the "sponge" and "gel" models. The sponge model postulates that cellulose particles provide the ability to hold water as a sponge (physically adsorbed water). During the extrusion process, these sponges are compressed until water is squeezed out and lubricates the particles flowing through the extruder. After extrusion, the volume of the sponges increases and the extrudate becomes dry and brittle (12), suggesting that the process did not alter the physicochemical properties of MCC. According to the sponge model, PC should be a suitable material for extrusion/spheronization. In contrast, the gel model proposes that, in the presence of water, MCC particles are broken down into smaller particles by shear forces acting on the particles during extrusion. Consequently, this breakdown will lead to an increase in the contact points between the cellulose fibers, resulting in a gel form; the gel network aids both extrusion and spheronization. Therefore, altering the particle size during extrusion is the critical parameter.

These results show a strong correlation between the DP and the particle size after homogenization, whereas no significant correlation between the DP and the apparent suspension viscosity could be made. The particle size after homogenization is comparable to the size of individual particles described by Ek et al (25). The presence of particles in the colloidal range was confirmed for different MCC types but not for PC by photon correlation spectroscopy in an earlier study (16).

The extrudate water content is strongly correlated with the DP of the MCC. Thus, another correlation exists between the particle size after homogenization and the water content during extrusion (Figure 7). The differences described between the different types of MCC include the experimental as well as commercially available types, meaning that the shear forces acting during the extrusion process result in a deformation of the initial particles. This reduction and/or deformation depends greatly on the DP of the cellulose types used. Cellulose with low DP displays a smaller particle size and vice versa. PC, which has the highest DP, shows a slight change in its particle sizes. A marked reduction in the particle size and/or enormous increase in the specific area greatly affects the water uptake and, consequently, the water content in the produced extrudates. Hence, it could be postulated that MCC extrudates resulted only from the formation of the gel network, whereas PC behaves more like a sponge.

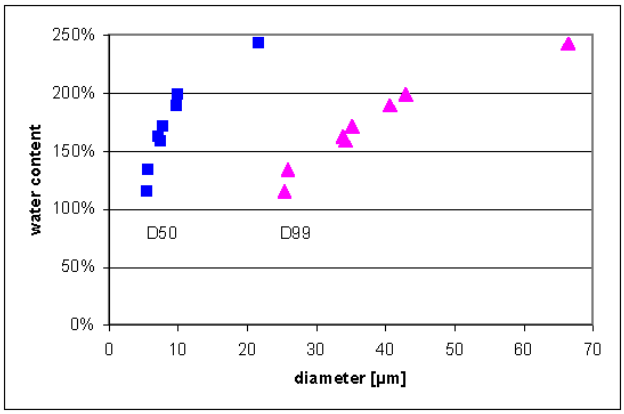

Figure 7. Correlation between particle size D_{50} and D_{99} of the various investigated cellulose types after homogenization (6 cycles, 40 MPa) with the extrudate water content.

Furthermore, when the sponge-like system is subjected to a drying process, a porous structure with a minor change in the size and shape results. In contrast, drying the gel-like system leads to an obvious shrinking behavior, leaving a less porous structure. This behavior is exactly what was observed after drying PC and MCC suspensions (Figure 4) as well as pellets (4,26). However, MCC is not an ideal gel, and PC is not an ideal sponge. There seems to be a full range of intermediate stages for different cellulose types, where MCC behaves in a more gel-like and PC in a more sponge-like manner. When MCC suspensions were not homogenized, the filter cakes showed no pronounced shrinking behavior. Thus, both the presence of water and the application of shear forces are necessary to form the gel-like structure of MCC.

The remarkable difference between PC and MCC must be explained by the different physical structure of the 2 cellulose types. PC has the highest DP and the lowest CI, resulting in the biggest particles after homogenization and the highest extrudate water content. PC undergoes a minor change in particle size during processing. Large particles with high DP and low CI show a more sponge-like behavior, perhaps because PC has a large hydrophilic amorphous region (low CI value) so that it can absorb a higher amount of water during extrusion inside the particles. PC particles, however, did not significantly agglomerate during the homogenization process. Therefore, no new contact points could be achieved. Hence, they are less prone to interact with each other to form a type network structure (this clearly can be seen from the agglomeration index value). Thus, they need more water (which is only physically adsorbed) to form a suitable and extrudable mass in order to obtain a successful extrusion process, which is actually very difficult.

The MCC types can physically adsorb smaller water amounts than PC because they have greater CI values and, consequently, a lower hydrophilic region (27). However, the water could be immobilized as a result of the particle size reduction (28). Moreover, this particle size reduction resulted in more contact points between the MCC fibers. Thus, the MCC particles are more prone to attract each other and, consequently, they showed a high agglomeration index. Hence, as more contact points are available, the formation of a satisfactory network can be achieved with a lower amount of water needed to obtain a suitable extrudable mass.

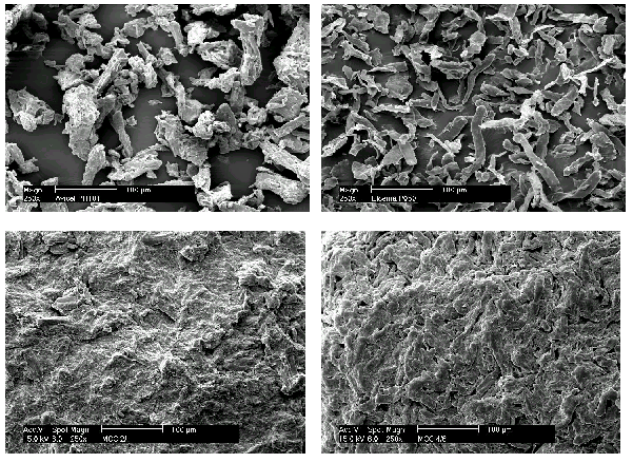

Figure 8. Scanning electron microscope pictures of the starting powders and the surface of the resulting pellets for DP225 (Avicel PH101) and DP1431 (Elcema P050).

These physically adsorbed and immobilized water types explained the different behaviors of MCC and PC preparations after the drying process. Removing the adsorbed water held between the cellulose fibers does not affect the size of the system, but it does result in a higher porosity. Conversely, removing the immobilized water results in an obvious shrinking, with major porosity changes (Figure 8). Thus, the network and also the appearance will be different in the case of extrudates produced with low DP types compared to the high DP types, as can clearly be seen in Figure 7.

Both powders show a rough structure with the obvious presence of fibers. Pellets produced using a low DP have a homogeneous surface, with only occasional fibers visible. Pellets made with a high DP are rougher, and oblong particles are visible on their surfaces. It seems as if they are formed from a bundle of fibers that are pressed and bound together. The

relatively homogeneous structure of MCC pellets is missing in this kind of pellet.

It might be predicted that a study using a ram extruder would show high water movement of these cellulose types compared to MCC types. This behavior makes a successful extrusion difficult. The increase in apparent viscosity after homogenization of PC suspensions cannot be explained.

In contrast, MCC is reduced in particle size during homogenization as well as in the process of granulation/extrusion/spheronization (16). The powder particles will not be reduced completely to colloidal particles, but they will be reduced mainly to the size of the crystallite aggregates and only partly to colloidal particles. In this sense, MCC behaves in a more "gel-like" manner, although a gel in the classical sense is not formed. As mentioned before, sponge and gel are images used to describe the extreme behavior possibilities for cellulose materials during extrusion and other processes. The reality seems to be somewhere in between, ie, more sponge-like behavior for PC and more gel-like behavior for MCC.

The reduction of extrudate water content with decreasing particle size contradicts the prediction of the crystallite gel model (8,13). This result was obtained in the comparison with different types of cellulose under the same process conditions. However, the prediction of an increase in water content during extrusion is valid for the comparison of different process conditions using the same type of cellulose. For 1 type of MCC, a range of structures is possible, depending on the applied forces and the water content.

Table 2 summarizes a comparison between the MCC and PC behavior during the extrusion and homogenization processes. This study can help to explain many of the observations concerning the extrusion/spheronization process. Consequently, this understanding of the extrusion process can assist in the production of suitable pellets with optimum properties when the physicochemical properties of the starting materials change.

Table 2. Comparison Between the Behavior of Cellulose With Low and High DP

Low DP (Gel Model)	High DP (Sponge Model)
Marked reduction in the particle size	Small reduction in the particle size
Less water needed (immobilized water)	More water needed (absorbed water)
Deformation of MCC during the extrusion process	No deformation of MCC during the extrusion process
More shrinking during the drying process	Less shrinking during the drying process
Low porosity of dried pellets	High porosity of dried pellets

CONCLUSIONS

For the first time, it was seen that altering the physical properties of cellulose material (especially the DP) resulted in a great change in the behavior of the material during the homogenization and extrusion processes. Consequently, this alteration can aid in the production of pellets with different properties. It is also proposed that the sponge model is more appropriate for the cellulose type with high DP (PC), whereas the gel model is better able to explain the behavior of cellulose types with lower DP (MCC). Thus, results published for native cellulose cannot be applied directly to MCC because of different DP values.

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